Patent claims.

1.   A method for the methylation analysis, characterized by that

a) a genome-wide amplification is performed,

b) the amplificates generated in a) are used as a standard in the methylation analysis.

2.   The use of DNA produced by genome-wide amplification methods as a standard in the methylation analysis.

3.   A method or the use according to claim 1 or 2, characterized by that PEP, DOP-PCR or linker PCR are performed as an amplification method.

4.   A method or the use according to claim 1 or 2, characterized by that a multiple displacement amplification (MDA) is performed as an amplification method.

5.   A method or the use according to claim 4, characterized by that a φ29 polymerase is used in the MDA.

6.   A method or the use according to claim 4, characterized by that the MDA is performed by means of a commercially available kit.

7. A method or the use according to claim 6, characterized by that "GenomiPhi" (Amersham Biosciences) or "Repli-g" (Molecular Staging) is used as a kit.

8. A method or the use according to claim 4, characterized by that commercially available DNA produced by MDA is used as a standard.

9. A method or the use according to at least one of claims 1 - 8, characterized by that the methylation analysis is performed by restriction enzymes.

10. A method or the use according to at least one of claims 1 - 8, characterized by that the methylation analysis is performed after conversion of the DNA into a form, in which methylated cytosines can be distinguished from nonmethylated cytosines by means of hybridization, by methylation-specific ligation methods, MSP, Heavy Methyl or MethyLight.

11. A method or the use according to at least one of claims 1 - 8, characterized by that the methylation analysis is performed after conversion of the DNA into a form, in which methylated cytosines can be distinguished from nonmethylated cytosines by means of hybridization, by primer extension.

12. A method or the use according to at
least one of claims 1 - 11, characterized by
that the methylation analysis is performed after
conversion of the DNA into a form, in which me-
thylated cytosines can be distinguished from
non-methylated cytosines by means of hybridiza-
tion, by an amplification and a hybridization of
the amplificates at oligomer microarrays.

13. A method or the use according to at
least one of claims 1 - 12, characterized by
that the methylation analysis is performed after
conversion of the DNA into a form, in which me-
thylated cytosines can be distinguished from
non-methylated cytosines by means of hybridiza-
tion, by means of a multiplex PCR.

14. A method or the use according to at
least one of claims 1 - 13, characterized by
that a mixture of methylated and non-methylated
DNA is used as a standard.

15. A method or the use according to at
least one of claims 1 - 14, characterized by
that several mixtures of methylated and non-me-
thylated DNA with different shares of methylated
and non-methylated DNA are used as a standard.

16. A method or the use according to at
least one of claims 1 - 15, characterized by
that the methylation analysis is performed for
the diagnosis of cancer diseases or other dis-

eases associated with a modification of the methylation status.

17. A method or the use according to at least one of claims 1 - 16, characterized by that the methylation analysis is performed for the prognosis of desired or undesired effects of drugs and for the differentiation of cell types or tissues, or for the investigation of the cell differentiation.

18. A method for the determination of methylation rates of DNA samples by means of microarrays containing CG and TG oligomers, characterized by that

the arrays are hybridized with two calibration standards, which have defined methylation rates;

by using the obtained hybridization values, a calibration curve is determined by means of a suitable method of calculation, and

the actual methylation rates of the investigated DNA samples are determined by using this prepared calibration curve.

19. A method according to claim 18, characterized by that the two calibration standards have methylation rates of 0% and 100%, respectively.

20. A method according to claim 18, characterized by that more than two calibration standards are used, which have different methylation rates.

21. A method according to claim 18, characterized by that the actual methylation rates are determined in a multi-stage calculation process, characterized by that

a) a normalization of the hybridization values is performed, whereby methylation signals are determined,

b) a normalization of the signals is performed with the aim of variance stabilization,

c) the methylation rates are determined by using the calibration standards and a suitable maximum likelihood algorithm.

22. A method according to claim 21, characterized by that before the normalization, the hybridization values are corrected for the background noise inherent in the measurement method.

23. A kit comprising reagents for performing a WGA method or DNA amplified already by a WGA method and reagents for performing a bisulphite conversion, and optionally also containing a polymerase, primers and/or probes for an amplification and detection.

24. A methylated DNA produced by a WGA method and then methylated by means of an enzyme.

25. A methylated DNA produced by a WGA method and then methylated by means of the SssI methylase.

26. A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method.

27. A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method, wherein the share of methylated DNA is between 5 and 95%.

28. A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method, wherein the share of methylated DNA is between 10 and 80%.

29. A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method, wherein the share of methylated DNA is between 25 and 75%.

30. The use of the DNA according to claims 24 to 25 or of a mixture according to claims 26 to 29 for the methylation analysis.

31. A method or the use according to one of claims 1 to 17, wherein the genome-wide amplification is performed by exclusively using nucleotides or nucleotide triphosphates, respectively, which are non-methylated.

32. A kit comprising reagents for performing a WGA method by exclusively using non-methylated nucleotides or non-methylated nucleotide triphosphates, respectively, or genomic DNA amplified by exclusively using non-methylated nucleotides or non-methylated nucleotide triphosphates, respectively, by WGA method, reagents for performing a bisulphite conversion, and optionally at least one polymerase and primers for an amplification and/or probes for a detection.

33. An isolated methylated DNA or mixture of isolated methylated DNA fragments, respectively, obtainable by that genomic DNA is amplified by means of a WGA method by exclusively using non-methylated nucleotides or nucleotide triphosphates, respectively, and the amplified DNA or the mixture of amplified DNA fragments, respectively, is then methylated by means of an enzyme or the SssI methylase.

34. A mixture containing methylated and non-methylated DNA, preferably each from the same organism or from organisms of the same species, wherein the non-methylated DNA was obtained by means of a WGA method by using non-methylated nucleotides or nucleotide triphosphates, respectively, wherein optionally the share of methy-

lated DNA is in the range between 5 and 95 mole-%, in particular between 10 and 80 mole-%, preferably between 25 and 75 mole-%, related to the total content of DNA.